

AMENDMENTS TO THE SPECIFICATION

Please add the following to the specification after page 38, line 6:

--The current inventions may be further summarized and numbered in the following fashion (using 114 numbered Paragraphs) analogous to the procedure for numbering claims, where the word "Paragraph" has been substituted for the word "Claim":

1. A method of diagnosing, tracking a progression of, and/or determining the prognosis of a human or other mammal with a cancer said method comprising determining a level or presence of an angiocidin fragment, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE under non-reducing conditions.
2. The method of Paragraph 1, further comprising comparing the level of said angiocidin fragment against known values for healthy persons and/or against known values for metastatic or nonmetastatic tumors.
3. The method of Paragraph 1, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 376 amino acid residues in length.
4. The method of Paragraph 3, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 373 amino acid residues in length.
5. The method of Paragraph 4, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 340 amino acid residues in length.

6. The method of Paragraph 5, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 300 amino acid residues in length.
7. The method of Paragraph 6, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 250 amino acid residues in length.
8. The method of Paragraph 7, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 200 amino acid residues in length.
9. The method of Paragraph 8, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 150 amino acid residues in length.
10. The method of Paragraph 9, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 100 amino acid residues in length.
11. The method of Paragraph 10, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 50 amino acid residues in length.
12. The method of Paragraph 11, wherein the purified angiocidin fragment is not less than four amino acid residues in length and not more than 25 amino acid residues in length.
13. The method of Paragraph 1, wherein the level of the angiocidin fragment is analyzed from a sample of bodily fluid or from a biopsy.
14. The method of Paragraph 13, wherein the bodily fluid is selected from the group consisting of blood, blood plasma, serum, lymph, cerebrospinal fluid, ascites fluid, urine, a lavage fluid, blister fluid, tears, saliva, a secretion, a mucous fluid, bile, milk, an aspirate, and a cyst fluid.

15. The method of Paragraph 13, wherein analysis of the biopsy comprises a step selected from the group of immunohistochemical staining, immunofluorescent staining, immune staining, nonimmune staining, and an assay of the biopsy or an extract thereof.

16. A method of diagnosing, tracking a progression of, and/or determining the prognosis of a mammal with a cancer said method comprising determining a level or presence of an aggregate containing angiocidin or a fragment thereof, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE under non-reducing conditions.

17. The method of Paragraph 16, wherein the aggregate is more than 60 kD in molecular weight.

18. The method of Paragraph 16, wherein the aggregate comprises a homodimer, a heterodimer, or a higher order complex.

19. The method of Paragraph 16, wherein the aggregate is formed by a process selected from the group consisting of self-aggregation, aggregation with another angiocidin molecule, aggregation of more than one angiocidin fragment, aggregation of an angiocidin fragment with a fragment of a molecule that is not angiocidin, aggregation of an angiocidin fragment with a molecule that is not a fragment, sulphydryl linkage with a second molecule or fragment, covalent linkage of angiocidin with another molecule or moiety, ionic linkage of angiocidin with another molecule or moiety, hydrophobic association of angiocidin with another molecule or moiety, homodimerization, heterodimerization and formation of a higher order complex.

20. The method of Paragraph 16, wherein the level of the angiocidin aggregate is analyzed from a sample of bodily fluid or from a biopsy.

21. The method of Paragraph 20, wherein the bodily fluid is selected from the group consisting of blood, blood plasma, serum, lymph, cerebrospinal fluid, ascites fluid, urine, a lavage fluid, blister fluid, tears, saliva, a secretion, a mucous fluid, bile, milk, an aspirate, and a cyst fluid.
22. The method of Paragraph 20, wherein analysis of the biopsy comprises a step selected from the group of immunohistochemical staining, immunofluorescent staining, immune staining, nonimmune staining, and an assay of the biopsy or an extract thereof.
23. The method of Paragraph 20, wherein analysis of the biopsy comprises an assay of a homogenated tissue and the level of the angiocidin fragment is normalized to a volume of sample and/or an amount of a protein and/or total protein and/or its level in a control sample.
24. The method of Paragraph 23, wherein the control sample is a housekeeping molecule.
25. The method of Paragraph 24, wherein the housekeeping molecule is selected from the group consisting of actin, cyclophilin, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), 18S, and total protein.
26. The method of Paragraph 1, wherein the method comprises a step wherein the fragment is physically separated from angiocidin, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTCG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE.
27. The method of Paragraph 1, wherein the mammal is a human.

28. A method that distinguishes two angiocidin fragments from each other, said fragments being a first fragment and a second fragment, respectively, said method comprising the steps of:

- (1) utilizing an epitope or binding target shared by said first fragment and said second fragment as a target for a binding agent to obtain a quantitation of a total of said first fragment plus said second fragment;
- (2) utilizing an epitope or binding target present in said first fragment but not present in said second fragment, to obtain a quantitation of said first fragment only; and
- (3) utilizing the difference between the quantitations in steps (1) and (2) as a quantitation of the amount of said second fragment.

29. The method of Paragraph 28, wherein the method comprises a step wherein the fragment is physically separated from angiocidin, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTCG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE.

30. The method of Paragraph 28, wherein the physical separation is accomplished using a technique that is selected from the group consisting of gel electrophoresis, dialysis, chromatography, size chromatography, affinity chromatography, immunoaffinity chromatography, adsorption, immunoadsorption, isoelectric focusing, mass spectrometry, centrifugation, sedimentation, floatation, precipitation, immunoprecipitation, extraction, and gel filtration.

31. The method of Paragraph 28, wherein the bodily fluid is selected from the group consisting of blood, blood plasma, serum, lymph, cerebrospinal fluid, ascites fluid, urine, a lavage fluid, blister fluid, tears, saliva, a secretion, a mucous fluid, bile, milk, an aspirate, and cyst fluid.

32. A method of detecting a presence and/or a clinical course of a neoplastic disease by assaying a bodily fluid from an individual, wherein the method comprises the steps of:

- (1) measuring the individual's bodily fluid level of an angiocidin fragment;
- (2) utilizing the result of step (1) in a diagnosis as to whether the individual has a neoplastic disease and/or whether a known neoplastic disease has progressed, regressed, or remained stable.

33. The method of Paragraph 32, wherein the bodily fluid is selected from the group consisting of blood, blood plasma, serum, lymph, cerebrospinal fluid, ascites fluid, urine, a lavage fluid, blister fluid, tears, saliva, a secretion, a mucous fluid, bile, milk, an aspirate, and a cyst fluid.

34. The method of Paragraph 32, wherein the neoplastic disease is selected from the group consisting of an adenoma, an adenocarcinoma, a carcinoma, a lymphoma, a leukemia, a skin cancer, a sarcoma, and an internal cancer.

35. The method of Paragraph 32, wherein the individual referred to therein is a first individual and wherein the method further comprises the steps of:

- (3) measuring a second individual's level of the angiocidin fragment in the same type of bodily fluid utilized for step (1), said second individual considered to not have neoplastic disease; and
- (4) utilizing the result of step (3) in the diagnosis of whether the first individual has a neoplastic disease.

36. The method of Paragraph 32, wherein the first individual's angiocidin fragment level exceeds the angiocidin fragment level of the second individual, and this difference is used to conclude that it is more likely that the diagnosis will be that the first individual has a neoplastic disease and/or a neoplastic disease more advanced than that of the second individual.

37. The method of Paragraph 32, further comprising the steps of assaying the individual's bodily fluid level for an angiocidin fragment more than once, and considering utilizing a change in bodily fluid level from an older to a more recent value to indicate appearance or progression or improvement, wherein said appearance, progression or improvement is indicated by an increase in the level of said angiocidin fragment and said improvement is indicated by a decrease in said level.

38. The method of Paragraph 37, wherein the bodily fluid level of an angiocidin fragment is assayed on 2 or more days.

39. The method of Paragraph 37, wherein the bodily fluid level of an angiocidin fragment is assayed on 3 or more days spaced at regular intervals, said intervals ranging from two weeks to ten years.

40. The method of Paragraph 32, wherein the neoplastic disease is selected from the group consisting of an adenoma, an adenocarcinoma, a carcinoma, a lymphoma, a leukemia, a skin cancer, a sarcoma, and an internal cancer.

41. The method of Paragraph 32, wherein the neoplastic disease is an internal cancer.

42. The method of Paragraph 32, wherein the neoplastic disease is selected from the group consisting of a cancer of the respiratory system, a cancer of the circulatory system, a cancer of the musculoskeletal system, a cancer of a muscle, a cancer of a bone, a cancer of a joint, a cancer of a tendon and/or ligament, a cancer of a connective tissue, a cancer of the digestive system, a cancer of the liver and/or biliary system, a cancer of the pancreas, a cancer of the head, a cancer of the neck, a cancer of the endocrine system, a cancer of the reproductive system, a cancer of the male reproductive system, a cancer of the female reproductive system, a cancer of the genitourinary system, a cancer of a kidney, a cancer of the urinary tract, a skin

cancer, a cancer of another sensory organ, a cancer of the nervous system, a cancer of a lymphoid organ, a blood cancer, a cancer of a gland, a cancer of a mammary gland, a cancer of a prostate gland, a cancer of endometrial tissue, a cancer of mesodermal tissue, a cancer of ectodermal tissue, cancer of an endodermal tissue, a teratoma, a poorly-differentiated cancer, a well-differentiated cancer, and a moderately differentiated cancer.

43. The method of Paragraph 32, wherein the neoplastic disease is selected from the group consisting of a cancer of solid tissue, a cancer of the blood or the lymphatic system, a solid cancer, a liquid cancer, a non-metastatic cancer, a premetastatic cancer, a metastatic cancer, a cancer with vascular invasion, a skin cancer, a poorly differentiated cancer, a well-differentiated cancer and a moderately differentiated cancer.

44. The method of Paragraph 32, wherein the measurement of an angiocidin fragment level comprises a use of a binding agent, said binding agent being capable of binding said fragment.

45. The method of Paragraph 44, wherein said method comprises the use of a first binding agent, said first binding agent capable of binding angiocidin but not the angiocidin fragment, and further comprises a second binding agent, said binding agent capable of binding angiocidin and capable of binding the angiocidin fragment.

46. The method of Paragraph 44, wherein said binding agent comprises a protein and/or a polypeptide.

47. The method of Paragraph 44, wherein said binding agent comprises an antibody or another molecule that crossreacts with or binds to an angiocidin fragment.

48. The method of Paragraph 47, wherein said antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, and single-chain antibody.

49. The method of Paragraph 46, wherein said protein comprises an antibody fragment.

50. The method of Paragraph 47, wherein said binding agent comprises a non-protein.

51. The method of Paragraph 46, wherein said protein and/or polypeptide is derived from a phage display library.

52. The method of Paragraph 44, wherein said binding agent is selected from the group consisting of an aptamer, a DNA, an RNA, a modified DNA, a modified RNA, a carbohydrate, a glycosaminoglycan, a heparin, a glycoprotein, a proteoglycan, and combinations and derivatives thereof.

53. A method of Paragraph 44, wherein said binding agent comprises a ligand that binds an angiocidin fragment and another molecule, where said molecule contains an epitope that is present in an angiocidin fragment and/or aggregate in a sample.

54. The method of Paragraph 53, wherein said ligand is selected from the group consisting of a thrombospondin, a thrombospondin fragment that binds angiocidin, a molecule comprising a thrombospondin fragment sequence that binds angiocidin, and a molecule comprising the amino acid sequence CSVTCG (SEQ ID NO:3).

55. The method of Paragraph 32, wherein said measuring the individual's bodily fluid level of an angiocidin fragment or fragments further comprises the use of an angiocidin fragment as a standard.

56. The method of Paragraph 55, wherein said angiocidin fragment used as a standard is selected from the group consisting of a recombinant angiocidin fragment, a purified angiocidin fragment that occurs in a bodily fluid, a purified angiocidin fragment that occurs in a mixture

with other angiocidin fragments, a partially purified angiocidin fragment, a synthetic angiocidin fragment, and an angiocidin fragment that contains an epitope that is present in an angiocidin fragment in a sample from a cancer patient.

57. The method of Paragraph 44, wherein the angiocidin fragment is separated from angiocidin before said angiocidin fragment is bound to the binding agent, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTCG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE under non-reducing conditions.

58. A method of detecting a presence and/or a clinical course of a neoplastic disease by assaying a bodily fluid from an individual, wherein the method comprises the steps of:

(1) measuring the individual's bodily fluid level of an angiocidin aggregate; and

(2) utilizing the result of step (1) in a diagnosis as to whether the individual has a neoplastic disease and/or whether a known neoplastic disease has progressed, regressed, or remained stable.

59. The method of Paragraph 58, wherein the bodily fluid is selected from the group consisting of blood, blood plasma, serum, lymph, cerebrospinal fluid, ascites fluid, urine, a lavage fluid, blister fluid, tears, saliva, a secretion, a mucous fluid, bile, milk, an aspirate, and a cyst fluid.

60. The method of Paragraph 58, wherein the individual referred to therein is a first individual and wherein the method further comprises the steps of:

(3) measuring a second individual's level of the angiocidin aggregate in the same type of bodily fluid utilized for step (1), said second individual considered to not have neoplastic disease; and

(4) utilizing the result of step (3) in the diagnosis of whether the first individual has a

neoplastic disease.

61. The method of Paragraph 60, wherein the first individual's angiocidin aggregate level exceeds the angiocidin aggregate level of the second individual, and this difference is used to conclude that it is more likely that the diagnosis will be that the first individual has a neoplastic disease and/or a neoplastic disease more advanced than that of the second individual.

62. The method of Paragraph 61, further comprising the steps of assaying the individual's bodily fluid level for an angiocidin aggregate more than once, and considering utilizing a change in bodily fluid level from an older to a more recent value to indicate appearance or progression or improvement, wherein said appearance or progression is indicated by an increase in the level of said angiocidin aggregate, and said improvement is indicated by a decrease in said level.

63. The method of Paragraph 62, wherein the bodily fluid level of an angiocidin aggregate is assayed on 2 or more days.

64. The method of Paragraph 62, wherein the bodily fluid level of an angiocidin aggregate is assayed on 3 or more days spaced at regular intervals, said intervals ranging from two weeks to ten years.

65. The method of Paragraph 58, wherein the neoplastic disease is selected from the group consisting of an adenoma, an adenocarcinoma, a carcinoma, a lymphoma, a leukemia, a skin cancer, an internal cancer, and a sarcoma.

66. The method of Paragraph 58, wherein the neoplastic disease is an internal cancer.

67. The method of Paragraph 58, wherein the neoplastic disease is selected from the group consisting of a cancer of the respiratory system, a cancer of the circulatory system, a cancer of the musculoskeletal system, a cancer of a muscle, a cancer of a bone, a cancer of a

joint, a cancer of a tendon and/or ligament, a cancer of a connective tissue, a cancer of the digestive system, a cancer of the liver and/or biliary system, a cancer of the pancreas, a cancer of the head, a cancer of the neck, a cancer of the endocrine system, a cancer of the reproductive system, a cancer of the male reproductive system, a cancer of the female reproductive system, a cancer of the genitourinary system, a cancer of a kidney, a cancer of the urinary tract, a skin cancer, a cancer of another sensory organ, a cancer of the nervous system, a cancer of a lymphoid organ, a blood cancer, a cancer of a gland, a cancer of a mammary gland, a cancer of a prostate gland, a cancer of endometrial tissue, a cancer of mesodermal tissue, a cancer of ectodermal tissue, cancer of an endodermal tissue, a teratoma, a poorly-differentiated cancer, a well-differentiated cancer, and a moderately differentiated cancer.

68. The method of Paragraph 58, wherein the neoplastic disease is selected from the group consisting of a cancer of solid tissue, a cancer of the blood or the lymphatic system, a solid cancer, a liquid cancer, a non-metastatic cancer, a premetastatic cancer, a metastatic cancer, a cancer with vascular invasion, a skin cancer, a poorly differentiated cancer, a well-differentiated cancer and a moderately differentiated cancer.

69. The method of Paragraph 58, wherein the measurement of an angiocidin aggregate level comprises a use of a binding agent, said binding agent being capable of binding said aggregate.

70. The method of Paragraph 69, wherein said method comprises the use of a first binding agent, said first binding agent capable of binding angiocidin but not the angiocidin aggregate, and further comprises a second binding agent, said binding agent capable of binding angiocidin and capable of binding the angiocidin aggregate, wherein angiocidin is a molecule comprising SEQ ID NO:1 or SEQ ID NO:2 and/or a molecule that binds thrombospondin through its CSVTCG (SEQ ID NO: 3) peptide domain and has an apparent molecular weight of 50 kD in an SDS-PAGE gel under non-reducing conditions.

71. The method of Paragraph 69, wherein said binding agent comprises a protein and/or a polypeptide.

72. The method of Paragraph 69, wherein said binding agent comprises an antibody or another molecule that crossreacts with or binds to an angiocidin aggregate.

73. The method of Paragraph 72, wherein said antibody is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, and single-chain antibody.

74. The method of Paragraph 71, wherein said protein comprises an antibody fragment.

75. The method of Paragraph 69, wherein said binding agent comprises a non-protein.

76. The method of Paragraph 71, wherein said protein and/or polypeptide is derived from a phage display library.

77. The method of Paragraph 69, wherein said binding agent is selected from the group consisting of an aptamer, a DNA, an RNA, a modified DNA, a modified RNA, a carbohydrate, a glycosaminoglycan, a heparin, a glycoprotein, a proteoglycan, and combinations and derivatives thereof.

78. A method of Paragraph 69, wherein said binding agent comprises a ligand that binds angiocidin or an angiocidin aggregate.

79. The method of Paragraph 78, wherein said ligand is selected from the group consisting of a thrombospondin, a thrombospondin aggregate that binds angiocidin, a molecule comprising a thrombospondin aggregate sequence that binds angiocidin, and a molecule comprising the amino acid sequence CSVTCG (SEQ ID NO:3).

80. The method of Paragraph 58, wherein said measuring the individual's bodily fluid level of an angiocidin aggregate further comprises the use of an angiocidin aggregate as a standard.

81. The method of Paragraph 80, wherein said angiocidin aggregate used as a standard is a purified angiocidin aggregate that occurs in a bodily fluid, a purified angiocidin aggregate that occurs in a mixture with other angiocidin aggregates, and a partially purified angiocidin aggregate.

82. The method of Paragraph 58, wherein the angiocidin aggregate is separated from angiocidin before said angiocidin aggregate is bound to the binding agent.

83. A polypeptide, the amino acid sequence of said polypeptide being one that is at least 4 amino acids in length and that is comprised of either a portion of SEQ ID NO:1 or a portion of SEQ ID NO:2, such that 1-10% of an N-terminus and/or 1-10% of a C-terminus of SEQ ID NO:1 is excluded from said portion of SEQ ID NO:1 and such that 1-10% of an N-terminus and/or a C-terminus of SEQ ID NO:2 is excluded from said portion of SEQ ID NO:2.

84. A polypeptide, said polypeptide selected from the group consisting of (1) a polypeptide comprised of SEQ ID NO:1 provided that a portion of SEQ ID NO:1 is missing in the polypeptide, said missing portion selected from the group consisting of a signal peptide, a membrane association sequence, and a cell association sequence, and (2) a polypeptide comprised of SEQ ID NO:2 provided that a portion of SEQ ID NO:2 is missing in the polypeptide, said missing portion selected from the group consisting of a signal peptide, a membrane association sequence, and a cell association sequence.

85. A polypeptide, the amino acid sequence of said polypeptide being one that is at least 4 amino acids in length and that is comprised of either a portion of SEQ ID NO:1 or a portion of SEQ ID NO:2, such that 5-15% of the N-terminus and/or C-terminus of SEQ ID NO:1 is

excluded from said portion of SEQ ID NO:1 and such that 5-15% of the N-terminus and/or C-terminus of SEQ ID NO:2 is excluded from said portion of SEQ ID NO:2.

86. A polypeptide, the amino acid sequence of said polypeptide being one that is at least 4 amino acids in length and that is comprised of either a portion of SEQ ID NO:1 or a portion of SEQ ID NO:2, such that 10-25% of an N-terminus and/or a C-terminus of SEQ ID NO:1 is excluded from said portion of SEQ ID NO:1 and such that 10-25% of an N-terminus and/or a C-terminus of SEQ ID NO:2 is excluded from said portion of SEQ ID NO:2.

87. A polypeptide, the amino acid sequence of said polypeptide being one that is at least 4 amino acids in length and that is comprised of either a portion of SEQ ID NO:1 or a portion of SEQ ID NO:2, such that 15-45% of an N-terminus and/or a C-terminus of SEQ ID NO:1 is excluded from said portion of SEQ ID NO:1 and such that 15-45% of an N-terminus and/or a C-terminus of SEQ ID NO:2 is excluded from said portion of SEQ ID NO:2.

88. A purified angiocidin fragment that has been extracted from a bodily fluid, said fragment being one within a molecular weight range of 10 to 50 kD, wherein the size in kD is that determined by gel electrophoresis after disulfide bond reduction.

89. A purified angiocidin aggregate that has been extracted from bodily fluid, said aggregate being one with a molecular weight range greater than 60 kD, wherein the size in kD is that determined by gel electrophoresis after disulfide bond reduction.

90. A method of producing an antibody against an angiocidin fragment of Paragraph 83 or an angiocidin aggregate of Paragraphs 84, 85, 86, 87, 88 or 89, said method comprising administering said fragment, aggregate or immunogenic portion thereof to an organism capable of producing antibodies.

91. The method of Paragraph 90, wherein a polyclonal antibody is produced.

92. The method of Paragraph 90, wherein a monoclonal antibody is produced.

93. An antibody produced by the method of Paragraph 90.

94. A cell line producing the monoclonal antibody of Paragraph 92.

95. The cell line of Paragraph 94, wherein said cell line is selected from the group consisting of a hybridoma, a transfected cell line, and an infected cell.

96. A method of producing a peptide or non-peptide binding agent against an angiocidin fragment of Paragraph 83, 84, 85, 86, 87, 88 or 89 an angiocidin aggregate of Paragraph 108, or epitope therein, said method comprising the steps of

- 1) a generating step (random, semi-random, directed, combinatorial, and/or other) to generate large numbers (>100) of diverse peptides and/or non-peptides;
- 2) a selection step to identify within this large number those peptides and/or non-peptides that bind to the angiocidin fragment, angiocidin aggregate and/or an epitope therein; and
- 3) optionally an improvement step for improving the peptide or non-peptide binding agent to achieve better affinity and/or specificity.

97. The method of Paragraph 96, wherein the binding agent is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, a single-chain antibody, a non-antibody, a protein, a product of phage display, an aptamer, a DNA, an RNA, a modified DNA, a modified RNA, a carbohydrate, a glycosaminoglycan, a heparin, a glycoprotein, a proteoglycan, and combinations and derivatives thereof.

98. The method of Paragraph 96, wherein the optional step for improving the binding agent is selected from the group consisting of molecular evolution, mutation of crucial residues, making dimeric, trimeric or multimeric molecules, and incorporation of sequences from animals

or humans exposed to or expressing antibodies against the fragment or epitope therein.

99. The method of Paragraph 96, wherein the initial set of diverse molecules is enriched by using sequences from animals or humans exposed to or expressing antibodies against the target.

100. A cell line capable of producing a binding agent produced by the method of Paragraph 96.

101. The cell line of Paragraph 100, wherein said cell line is selected from the group consisting of a hybridoma, a transfected cell line, and an infected cell.

102. A method of diagnosing, tracking a progression of, and/or determining the prognosis of a human or other mammal with a cancer said method comprising reacting a sample from a patient with an antibody or other binding agent, wherein said antibody or binding agent is reactive with an epitope or binding target present in angiocidin and/or an angiocidin fragment and/or an angiocidin aggregate.

103. The method of Paragraph 102, wherein the total amount of material reactive with the antibody or other binding agent is quantitated.

104. The method of Paragraph 102, wherein the epitope and/or binding target is present in angiocidin.

105. The method of Paragraph 102, wherein the epitope and/or binding target is present in an angiocidin fragment.

106. The method of Paragraph 102, wherein the epitope and/or the binding target is present in an angiocidin aggregate.

107. A method that distinguishes two angiocidin fragments from each other, said fragments being a first fragment and a second fragment, respectively, said method comprising the steps of: utilizing an epitope or binding target present in said first fragment but not present in said second fragment, to obtain a quantification of said first fragment only.

108. A method of generating an antibody reactive with an angiocidin fragment, said method comprising use of an angiocidin fragment as an immunogen.

109. A method of generating a binding agent reactive with an angiocidin fragment, said method comprising the use of an angiocidin fragment.

110. A method of diagnosing, tracking a progression of, and/or determining the prognosis of a human or other mammal with a disease or condition said method comprising determining a level or presence of an angiocidin fragment, wherein angiocidin is a molecule selected from the group consisting of a molecule whose amino acid sequence is SEQ ID NO:1, a molecule whose amino acid sequence is SEQ ID NO:2, and a molecule that binds to the CSVTG (SEQ ID NO: 3) peptide domain of thrombospondin and has a measured molecular weight of about 50 kD when subjected to an SDS-PAGE under non-reducing conditions.

111. The method of Paragraph 110, wherein the disease or condition is a disease.

112. The method of Paragraph 110, wherein the disease or condition is a condition.

113. A method of detecting a presence and/or a clinical course of a neoplastic disease by assaying a bodily fluid from an individual, wherein the method comprises the steps of:

(1) measuring the individual's bodily fluid level of an angiocidin fragment epitope;

(2) utilizing the result of step (1) in a diagnosis as to whether the individual has a

neoplastic disease and/or whether a known neoplastic disease has progressed, regressed, or remained stable.

114. The method of Paragraph 113, wherein the individual referred to therein is a first individual and wherein the method further comprises the steps of:

(3) measuring a second individual's level of the angiocidin fragment epitope in the same type of bodily fluid utilized for step (1), said second individual considered to not have neoplastic disease; and

(4) utilizing the result of step (3) in the diagnosis of whether the first individual has a neoplastic disease.